

Applicants: Philip O. Livingston and Friedhelm Helling
Serial No.: 08/477,147
Filed: June 7, 1995
Page 2

Please amend the subject application as follows:

Amendment to the Claims:

This listing of claims will replace all prior versions,
and listings, of claims in the application:

Listing of the Claims:

1.-122. (Cancelled)

123. (Currently Amended) A composition which comprises:

a) a conjugate of (i) a derivative of a ganglioside, which ganglioside (1) is a GM2, GD2, GD3 lactone, O-acetyl GD3, or GT3 ganglioside and (2) comprises an unaltered sphingosine base, wherein the derivative differs from the ganglioside solely by having an altered sphingosine base which retains only C1 through C4 from the unaltered sphingosine base of the ganglioside, and (ii) Keyhole Limpet Hemocyanin, wherein the ganglioside derivative is covalently bound to Keyhole Limpet Hemocyanin by a stable amine bond between the C-4 carbon of the altered sphingosine base and a nitrogen of an ϵ -aminolysyl group of Keyhole Limpet Hemocyanin;

b) QS-21; and

c) a pharmaceutically acceptable carrier;

wherein the amount of the conjugated ganglioside derivative is an amount between about 1 µg and about 200 µg, the amount of QS-21 is an amount between about 10 µg and about 200 µg, the ganglioside derivative:Keyhole Limpet Hemocyanin molar ratio is from 200:1 to 1400:1, and the relative amounts of such conjugate and QS-21 is effective to stimulate or enhance production in a subject of an antibody to the ganglioside, ~~the derivative of which is present in the conjugate.~~

124.-129. (Cancelled)

2 130. (Previously Presented) The composition of claim 123, wherein the amount of QS-21 is about 50 µg.

3 131. (Previously Presented) The composition of claim 123 wherein the amount of QS-21 is about 200 µg.

4 132. (Currently Amended) The composition of claim 123 which comprises:

a) a conjugate of (i) a derivative of a ganglioside, which ganglioside (1) is a GM2, GD2, GD3 lactone, O-acetyl GD3, or GT3 ganglioside and (2) comprises an unaltered sphingosine base, wherein the derivative differs from the ganglioside solely by having an altered sphingosine base which retains only C1 through C4 from the unaltered

sphingosine base of the ganglioside, and (ii) Keyhole Limpet Hemocyanin, wherein the ganglioside derivative is covalently bound to Keyhole Limpet Hemocyanin by a stable amine bond between the C-4 carbon of the altered sphingosine base and a nitrogen of an ϵ -aminolysyl group of Keyhole Limpet Hemocyanin;

b) QS-21; and

c) a pharmaceutically acceptable carrier;

wherein the amount of the conjugated ganglioside derivative is an amount between about 1 μ g and about 200 μ g, and the amount of QS-21 is about 100 μ g, the ganglioside derivative:Keyhole Limpet Hemocyanin molar ratio is from 200:1 to 1400:1, and ~~wherein~~ the relative amounts of such conjugate and QS-21 is effective to stimulate or enhance production in a subject of an antibody to GM2, GD2, GD3 and GT3, ~~the ganglioside, the derivative of which is present in the conjugate.~~

§ 133. (Previously Presented) A method of treating a subject afflicted with melanoma which comprises administering to said subject an amount of a composition of claim 132 effective to stimulate or enhance production of an antibody to at least one ganglioside selected from the group consisting of GM2, GD2, GD3 lactone, O-acetyl GD3 and GT3 and to thereby treat said melanoma in said subject.

6 134. (Currently Amended) A method of stimulating or enhancing production of an antibody to GM2, GD2, GD3 and GT3 in a subject which comprises administering to the subject an effective amount of a composition which comprises:

a) a conjugate of (i) a derivative of a ganglioside, which ganglioside (1) is a GM2, GD2, GD3 lactone, O-acetyl GD3, or GT3 ganglioside and (2) comprises an unaltered sphingosine base, wherein the derivative differs from the ganglioside solely by having an altered sphingosine base which retains only C1 through C4 from the unaltered sphingosine base of the ganglioside, and (ii) Keyhole Limpet Hemocyanin, wherein the ganglioside derivative is covalently bound to Keyhole Limpet Hemocyanin by a stable amine bond between the C-4 carbon of the altered sphingosine base and a nitrogen of an ϵ -aminolysyl group of Keyhole Limpet Hemocyanin;

b) QS-21; and

c) a pharmaceutically acceptable carrier;

wherein the amount of the conjugated ganglioside derivative is an amount between about 1 μ g and about 200 μ g, the amount of QS-21 is an amount between about 10 μ g and about 200 μ g, and the

ganglioside derivative:Keyhole Limpet Hemocyanin
molar ratio is from 200:1 to 1400:1, the
~~ganglioside:Keyhole Limpet Hemocyanin~~, and the
relative amounts of such conjugate and QS-21 is
effective to stimulate or enhance production in a
subject of an antibody to GM2, GD2, GD3 and GT3,
the ganglioside, ~~derivative of which is in the~~
~~conjugate~~.

133. (Currently Amended) A method of treating a human
subject having cancer which comprises administering
to the subject an effective amount of a composition
which comprises:

a) a conjugate of (i) a derivative of a
ganglioside, which ganglioside (1) is a GM2,
GD2, GD3 lactone, O-acetyl GD3, or GT3
ganglioside and (2) comprises an unaltered
sphingosine base, wherein the derivative
differs from the ganglioside solely by having
an altered sphingosine base which retains
only C1 through C4 from the unaltered
sphingosine base of the ganglioside, and (ii)
Keyhole Limpet Hemocyanin;

b) QS-21; and

c) a pharmaceutically acceptable carrier;

wherein the amount of the conjugated ganglioside
derivative is an amount between about 1 µg and
about 200 µg, the amount of QS-21 is an amount

between about 10 μ g and about 200 μ g, the ganglioside derivative:Keyhole Limpet Hemocyanin molar ratio is from 200:1 to 1400:1, and the relative amounts of such conjugate and QS-21 is effective to stimulate or enhance production in a subject of an antibody to GM2, GD2, GD3 and GT3, the ganglioside, ~~the derivative of which is present in the conjugate.~~

- 8 136. (Previously Presented) The method of claim 135, wherein the cancer is of epithelial origin. 7
- 9 137. (Previously Presented) The method of claim 135, wherein the cancer is of neuroectodermal origin. 7
- 10 138. (Previously Presented) The method of claim 137, wherein the cancer of neuroectodermal origin is melanoma. 9
- 11 139. (Previously Presented) The method of claim 134 or 135, wherein the administering is effected at two or more sites. 6
- 12 140. (Previously Presented) The method of claim 139, wherein the administering is effected at three sites. 11
- 13 141. (Previously Presented) The method of claim 134 or 135, wherein the composition is administered subcutaneously to said subject. 6
- 14 142. (Previously Presented) The method of claim 141, 13

wherein the composition is administered to said subject at two-week intervals.

15 ~~143.~~ (Previously Presented) The method of claim 141, wherein the composition is administered to said subject at weekly intervals.

16 ~~144.~~ (Previously Presented) The method of claim 134 or 135, wherein the composition to be administered is prepared prior to administration to the subject by mixing the conjugate and QS-21.

17 ~~145.~~ (Previously Presented) The method of claim 144, wherein the conjugate and QS-21 are mixed on the day of administration to the subject.

146. (Cancelled)